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10/627,780	07/28/2003	Kejun Fan	240961US0	4288

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EXAMINER	
KIM, YOUNG J	

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 11/09/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/627,780	FAN, KEJUN	
	Examiner	Art Unit	
	Young J. Kim	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 August 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The present Office Action is responsive to the Amendment received on August 31, 2006.

Preliminary Remark

Claims 1-22 are pending and are under prosecution herein.

Applicants' statement regarding the Interview held on July 19, 2006 is accurate.

Claim Rejections - 35 USC § 112

The rejection of claim 6 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter, made in the Office Action mailed on May 31, 2006 is withdrawn in view of the Amendment received on August 31, 2006, amending the claim.

Claim Rejections - 35 USC § 102

The rejection of claims 1-6, 14, 15, and 17-22 under 35 U.S.C. 102(b) as being anticipated by Dzieglewska et al. (WO 98/51693, published November 19, 1998), made in the Office Action mailed on May 31, 2006 is withdrawn in view of the Amendment received on August 31, 2006.

Specifically, the instant claim amendment requires that the cells are first lysed with a lysis solution, followed by the step of bringing the sample containing the lysed cells into to contact with a water-insoluble solid phase carrier.

As Dzieglewska et al. lyse and bind the nucleic acids simultaneously, wherein the lysis of cells is effected by their contact with the water-insoluble solid phase carrier, such disclosure would not properly anticipate the instantly amended claims which require that the lysis step be conducted prior to the step of contacting the lysed cells with the water-insoluble solid support.

Rejection, Maintained

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The rejection of claims 1-6, 14, 15, and 17-22 under 35 U.S.C. 102(b) as being anticipated by Dzieglewska et al. (WO 98/51693, published November 19, 1998), made in the Office Action mailed on May 31, 2006 is maintained for the reasons of record.

Applicants' arguments presented in the Amendment received on August 31, 2006 have been fully considered but they are not found persuasive for the reasons set forth in the, "Response to Arguments" section.

The Rejection:

Dzieglewska et al. disclose a method of separating nucleic acid from a sample, comprising the steps:

a) bringing the sample containing the nucleated cells (eukaryotic cells, *see* page 4, lines 29-30) with a lysis solution containing at least a cellular component degrading enzyme and a surfactant (see page 11, lines 21 and 27, and the phrase, "any such method of combination of methods may be used");

b) bringing the sample containing nucleated cells into contact with a water-insoluble solid-phase carrier having an average particle size of 0.01 to 1000 μm (page 4, lines 7-10; page 9, lines 26-30) in the presence of a water-soluble organic solvent (page 6, lines 5-10) to adsorb and bind nucleic acids released from the nucleated cells onto the surface of the solid-phase carrier, thereby obtaining a solid-phase carrier having adsorbed nucleic acids (page 4, lines 4-5), and

c) separating the solid-phase carrier from the sample, thereby separating and purifying said nucleic acids (page 14, lines 31-35).

The cellular component-degrading enzyme is a protease (page 11, lines 26-29).

A surfactant is SDS, also known as sodium dodecyl sulfate (page 11, line 20-21).

The water-insoluble solid-phase carrier is glass, silica, latex or polymeric material (page 9, lines 17-18).

The artisans clearly contemplate a kit comprising the elements of the disclosed method (Abstract; page 19, line 12).

The water-soluble organic solvent is alcohol (page 6, line 9), more particularly, isopropanol or ethanol (page 9, line 16).

Therefore, Dzieglewska et al. clearly anticipate the invention as claimed.

Response to Arguments:

Applicants' arguments contending that the disclosed method of Dzieglewska et al. is different from the method of the instant claims is noted.

However, the presently rejected claim is drawn to a product – i.e., a kit.

A product is defined by its elements or reagents.

Dzieglewska et al. clearly contemplate a kit for conducing their method which requires at least a cellular component-degrading enzyme, a water-insoluble solid-phase carrier, a surfactant, and a water-soluble organic solvent.

The rejection is proper and the thus maintained.

Claim Rejections - 35 USC § 103

The rejection of claims 8-12 under 35 U.S.C. 103(a) as being unpatentable over Dzieglewka et al. (WO 98/51693, published November 19, 1998) in view of Ekeze et al. (EP 0 795 751 A2, published September 17, 1997), made in the Office Action mailed on May 31, 2006 is withdrawn in view of the Amendment received on August 31, 2006.

The rejection of claims 13 and 16 under 35 U.S.C. 103(a) as being unpatentable over Dzieglewska et al. (WO 98/51693, published November 19, 1998) in view of Belley et al. (U.S. Patent No. 6,469,159, issued October 22, 2002, filed April 26, 1999[1]), made in the Office Action mailed on May 31, 2006 is withdrawn in view of the Amendment received on August 31, 2006.

Rejections, New Grounds – Necessitated by Amendment

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-6, 14, 15, and 17-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dzieglewska et al. (WO 98/51693, published November 19, 1998) in view of Hayashizaki et al. (U.S. Patent No. 6,342,387, issued January 29, 2002, 102(e) date of June 12, 2000).

Dzieglewska et al. disclose a method of separating nucleic acid from a sample, comprising the steps:

a) bringing the sample containing the nucleated cells (eukaryotic cells, *see* page 4, lines 29-30) with a lysis solution containing at least a cellular component degrading enzyme and a surfactant (see page 11, lines 21 and 27, and the phrase, "any such method of combination of methods may be used");

b) bringing the sample containing nucleated cells into contact with a water-insoluble solid-phase carrier having an average particle size of 0.01 to 1000 μm (page 4, lines 7-10; page 9, lines 26-

[1] Already of record.

30) in the presence of a water-soluble organic solvent (page 6, lines 5-10) to adsorb and bind nucleic acids released from the nucleated cells onto the surface of the solid-phase carrier, thereby obtaining a solid-phase carrier having adsorbed nucleic acids (page 4, lines 4-5), and

c) separating the solid-phase carrier from the sample, thereby separating and purifying said nucleic acids (page 14, lines 31-35).

With regard to claim 2, the cellular component-degrading enzyme is a protease (page 11, lines 26-29).

With regard to claims 3 and 14, a surfactant is SDS, also known as sodium dodecyl sulfate (page 11, line 20-21).

With regard to claim 4, the water-insoluble solid-phase carrier is glass, silica, latex or polymeric material (page 9, lines 17-18).

With regard to claim 6, the artisans elute the nucleic acids (page 15, lines 27-34).

With regard to claims 15, 21, and 22, the artisans clearly state that for detergents, such as SDS, 0.5 to 15% detergents are to be employed (page 12, lines 18-19).

With regard to claims 17-19, the water-soluble organic solve is alcohol (page 6, line 9), more particularly, isopropanol or ethanol (page 9, line 16).

With regard to claim 20, the concentration of the water-soluble organic solvent is from 50-100% by volume (page 6, lines 25-26).

Dzieglewska et al. do not explicitly disclose that the lysis solution be applied to the sample comprising nucleated cells prior to contacting the lysed, nucleated cells to a solid phase.

Hayashizaki et al. explicitly disclose a method of purifying nucleic acids in a sample comprising nucleated cells (column 3, lines 10-13), wherein the artisans first apply a lysis solution to

said sample (column 2, lines 62-65), followed by their contact with a solid phase (or DNA-binding carrier) so as to bind the isolated nucleic acids thereto (column 2, line 65 through column 3, line 1).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Dzieglewska et al. with the teachings of Hayashizaki et al., thereby arriving at the invention as claimed for the following reasons.

While Dzieglewska et al. are not explicit in stating that their method first employ a lysis step, so as to produce lysed, nucleated cells, followed by their contact with the solid-phase carrier, the artisans clearly do not prohibit one from doing so. In addition, it would have been completely well within the purview of an ordinarily skilled artsian to separate the lysis and binding steps, so as to ensure that the cells are sufficiently lysed prior to their binding to the nucleic acid binding agent (i.e., solid-phase carrier).

Such knowledge is clearly demonstrated by Hayashizaki et al. who demonstrate the practice of conducting a lysis step prior to their contacting with a solid-phase carrier, in a method of isolating nucleic acids from a sample.

Specifically, Hayashizaki et al. recites the below (column 5, lines 41-51):

> The DNA-containing biological sample may be, for example, blood, a cell or a biological tissue. The cell may be a eukaryotic cell or a bacterial cell. Blood is a biological sample with laborious handleability, so that DNA isolation from blood is difficult by conventional methods. According to the method of the invention, DNA can be isolated therefrom. The concentration of a DNA-containing biological sample in the lysing solution can appropriately be determined, depending on the kind of the biological sample, the composition of the lysing solution and the kind of the DNA-binding carrier.

In addition, Hayashizaki et al. conduct a method comprising the steps of: lysing a sample (as discussed above), adding the lysate to a DNA-binding carrier, separating the DNA-bound carrier

from other components of the lysate, followed by dissociation of the DNA from the DNA-binding carrier.

Thus, one of ordinary skill in the art at the time the invention was made would have also had a clear expectation of success at employing the teachings of Dzieglewska et al. for conducting the lysis step prior to their contact with the DNA-binding carriers, as evidenced by Hayashizaki et al. for the purpose of ensuring a thorough lysis of the samples comprising nucleated cells, such as tissues, blood, etc., thereby arriving at the invention as claimed.

Claims 8-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dzieglewska et al. (WO 98/51693, published November 19, 1998) in view of Hayashizaki et al. (U.S. Patent No. 6,342,387, issued January 29, 2002, 102(e) date of June 12, 2000) as applied to claims 1-6, 14, 15, and 17-22 above, and further in view of Ekeze et al. (EP 0 795 751 A2, published September 17, 1997).

The teachings of Dzieglewska et al. and Hayashizaki et al. have already been discussed above.

Dzieglewska et al. and Hayashizaki et al., while explicitly contemplating that their method would be used in analyzing wide array of sample types, such as tissues, blood, blood-derived product, such as buffy coat (page 5, lines 9-10; Dzieglewska et al.; column 3, lines 11-13; Hayashizaki et al.), do not explicitly teach well known methods involved in treatment of each types of samples, particularly, with hemolytic agents.

Ekeze et al. disclose a well-known method of isolating nucleic acid from a blood sample, wherein the blood sample is treated with ammonium chloride, particularly in the concentration of 50 mM (or 0.05 M) (see page 3, lines 11-12).

It would have been *prima facie* obvious to one of ordinary skill in the art to employ the teachings of Dzieglewska et al. and Hayashizaki et al. for the purpose of isolating nucleic acids from

blood samples, wherein the artisans would have been clearly motivated to completely lyse the red-blood cells via well-known ammonium chloride treatment, so as to isolate the intact white blood cells from which to isolate the nucleic acids from, as evidenced by Ekeze et al.

With regard to the determination of the optimal conditions for recovering maximum amount of white blood cells, involving temperatures and ammonium chloride concentration, such is considered to be optimizing well-known conditions involving routine optimization.

MPEP 2144.05(II)(A) discloses that, "differences in concentrations or temperature ***will not support*** patentability of subject matter encompassed by prior art unless there is evidence indicating such concentration or temperature is critical," citing *In re Aller,* F.2d 454, 456, 105 USPQ 233, 235, (CCPA 1995).

Therefore, the invention as claimed is *prima facie* obvious over the cited references.

Claims 13 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dzieglewska et al. (WO 98/51693, published November 19, 1998) in view of Hayashizaki et al. (U.S. Patent No. 6,342,387, issued January 29, 2002, 102(e) date of June 12, 2000) as applied to claims 1-6, 14, 15, and 17-22 above, and further in view of Belley et al. (U.S. Patent No. 6,469,159, issued October 22, 2002, filed April 26, 1999).

The teachings of Dzieglewska et al. and Hayashizaki et al. have already been discussed above.

Dzieglewska et al., and Hayashizaki et al., while explicitly contemplating that their method would be used in analyzing wide array of sample types, such as tissues, blood, blood-derived product, such as buffy coat (page 5, lines 9-10; Dzieglewska et al; column 3, lines 11-13; Hayashizaki et al.), do not explicitly teach well known methods involved in treatment of each types of samples, particularly, tissues.

Belley et al. disclose a method of separating nucleic acid from paraffin embedded tissues (thus nucleated cells; *see* column 7, lines 45-46), wherein said method involves the steps: a) contacting the paraffin sample containing the nucleated cells with a lysis solution containing a protease (column 7, line 50; thus "a cellular component-degrading enzyme) and a surfactant (Tween20®; see column 7, line 49; column 4, lines 44-46; and claim 5).

Belley et al. explicitly disclose that the conditions involving the extraction involving their reagents are "readily determinable" by those of ordinary skill in the art. In particular, Belley et al. disclose the use of protease in extracting nucleic acid from tissues, wherein the conditions involve an incubation of the sample with the enzyme at 70° to 100° Celsius (column 4, lines 50-51).

With regard to the concentration of the enzyme, and its purity, such is clearly within the purview of an ordinarily skilled artisan in the art of nucleic acid extraction/isolation, the conditions of which would purely involve routine optimization.

MPEP 2144.05(II)(A) discloses that, "differences in concentrations or temperature ***will not support*** patentability of subject matter encompassed by prior art unless there is evidence indicating such concentration or temperature is critical," citing *In re Aller,* F.2d 454, 456, 105 USPQ 233, 235, (CCPA 1995).

Given the fact that the practice of employing proteases and temperature for extracting nucleic acids from tissue samples had been well known and established, finding an optimal concentration from which to operate from would only involve a routine experimentation of an ordinarily skilled artisan.

Therefore, the invention as claimed is *prima facie* obvious over the cited references.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Inquiries

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Young J. Kim whose telephone number is (571) 272-0785. The Examiner is on flex-time schedule and can best be reached from 8:30 a.m. to 4:30 p.m (M-W and F). The Examiner can also be reached via e-mail to Young.Kim@uspto.gov. However, the office cannot guarantee security through the e-mail system nor should official papers be transmitted through this route.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr. Gary Benzion, can be reached at (571) 272-0782.

Papers related to this application may be submitted to Art Unit 1637 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant does submit a paper by FAX, the original copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office. All official documents must be sent

to the Official Tech Center Fax number: (571) 273-8300. For Unofficial documents, faxes can be sent directly to the Examiner at (571) 273-0785. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Young J. Kim
Primary Examiner
Art Unit 1637
11/8/2006

YOUNG J. KIM
PRIMARY EXAMINER

YJK